

IN THE CLAIMS:

Applicants submit the following amendments to the claims pursuant to 37 C.F.R. § 1.121:

27. (Currently amended) A method for detecting cytosine methylation and methylated CpG islands within a genomic sample of DNA comprising:

(a) contacting a genomic sample of DNA with a modifying agent that modifies unmethylated cytosine to produce a converted nucleic acid;

(b) amplifying the converted nucleic acid by means of oligonucleotide primers in the presence of one or a plurality of specific oligonucleotide probes, wherein one or a plurality of the oligonucleotide primers or the specific probe(s) are capable of distinguishing between unmethylated and methylated nucleic acid, with the proviso that at least one oligonucleotide probe is a CpG-specific probe capable of distinguishing between unmethylated and methylated nucleic acid; and

(c) detecting the methylated nucleic acid based on at least one of an amplification-, mediated-, or amplification product-mediated displacement or conformational change of the CpG-specific probe; or an amplification-mediated-, or amplification product-mediated displacement or conformational change of the probe ~~change in a property of the CpG-specific probe, or in a property thereof~~ in relation to another probe or a primer.

28. (original) The method of claim 27 wherein the amplifying step is a polymerase chain reaction (PCR).

29. (original) The method of claim 27 wherein the modifying agent is bisulfite.

30. (original) The method of claim 27 wherein the converted nucleic acid contains uracil in place of unmethylated cytosine residues present in the unmodified nucleic acid-containing sample.

31. (original) The method of claim 27 wherein the probe further comprises one or a plurality of fluorescence label moieties.

32. (original) The method of claim 31 wherein the amplification and detection step comprises fluorescence-based quantitative PCR.

33. (Currently amended) The method of claim 31, wherein the probe is a FRET probe, or a dual-label hydrolysis probe comprising a fluorescence-reporter moiety and fluorescence-quencher moiety.

34. (Currently amended) The method of claim 33, wherein the FRET probe is one component of a real-time PCR ~~LightCycler™~~ ^{LightCycler™} type hybridization probe pair.

35. (Currently amended) The method of claim 33, wherein the ~~dual-label~~ probe is a dual-label hydrolysis ~~TaqMan™~~ ^{TaqMan™} type probe, or a molecular beacon-type probe.

36. (original) The method of claim 27, wherein at least one of the primers comprises a

CpG-specific probe.

37. (original) The method of claim 36, wherein the one primer is a scorpion-type primer comprising a CpG-specific probe that hybridizes to a target site within the scorpion primer extension product.

38. (Currently amended) A method for detecting a methylated CpG-containing nucleic acid comprising:

(a) contacting a nucleic acid-containing sample with a modifying agent that modifies unmethylated cytosine to produce a converted nucleic acid;

(b) amplifying the converted nucleic acid in the sample by means of oligonucleotide primers in the presence of a CpG-specific oligonucleotide probe, wherein the CpG-specific probe, but not the primers, distinguishes between modified unmethylated and methylated nucleic acid; and

(c) detecting the methylated nucleic acid based on at least one of an amplification-, mediated-, or amplification product-mediated displacement or conformational change of the CpG-specific probe; or an amplification-mediated-, or amplification product-mediated displacement or conformational change of the probe ~~change in a property of the CpG-specific probe, or in a property thereof~~ in relation to another probe or a primer.

39. (original) The method of claim 38 wherein the amplifying step comprises a polymerase chain reaction (PCR).

40. (original) The method of claim 38 wherein the modifying agent comprises bisulfite.

41. (original) The method of claim 38 wherein the converted nucleic acid contains uracil in place of unmethylated cytosine residues present in the unmodified nucleic acid-containing sample.

42. (original) The method of claim 38 wherein the probe further comprises one or a plurality of fluorescence label moieties.

43. (original) The method of claim 42 wherein the amplification and detection step comprises fluorescence-based quantitative PCR.

44. (Currently amended) The method of claim 42, wherein the probe is a FRET probe, or a dual-label hydrolysis probe comprising a fluorescence-reporter moiety and fluorescence-quencher moiety.

45. (Currently amended) The method of claim 44, wherein the FRET probe is one component of a real-time PCR ~~LightCyclerTM-type~~ hybridization probe pair.

46. (Currently amended) The method of claim 44, wherein the ~~dual-label~~ probe is a dual-label hydrolysis probe ~~TaqManTM-type~~ probe, or a molecular beacon-type probe.

47. (original) The method of claim 38, wherein at least one of the primers comprises a CpG-specific probe.

48. (original) The method of claim 47, wherein the one primer is a scorpion-type primer comprising a CpG-specific probe that hybridizes to a target site within the scorpion primer extension product.

49. (original) The method of claim 38 wherein methylation amounts in the nucleic acid sample are quantitatively determined based on reference to a control reaction for amount of input nucleic acid.

50. (Currently amended) A method for detecting a methylated CpG-containing nucleic acid comprising:

(a) contacting a nucleic acid-containing sample with a modifying agent that modifies unmethylated cytosine to produce a converted nucleic acid;

(b) amplifying the converted nucleic acid in the sample by means of oligonucleotide primers in the presence of a CpG-specific oligonucleotide probe, wherein both the primers and the CpG-specific probe distinguish between modified unmethylated and methylated nucleic acid; and

(c) detecting the methylated nucleic acid based on at least one of an amplification-, mediated-, or amplification product-mediated displacement or conformational change of the CpG-specific probe; or an amplification-mediated-, or amplification product-mediated displacement or conformational change of the probe ~~change in a property of the CpG-specific probe, or in a property thereof~~ in relation to another probe or a primer.

51. (original) The method of claim 50 wherein the amplifying step comprises a polymerase chain reaction (PCR).

52. (original) The method of claim 50 wherein the modifying agent is bisulfite.

53. (original) The method of claim 50 wherein the converted nucleic acid contains uracil in place of unmethylated cytosine residues present in the unmodified nucleic acid-containing sample.

54. (original) The method of claim 50 wherein the probe further comprises one or a plurality of fluorescence label moieties.

55. (original) The method of claim 54 wherein the amplification and detection step comprises fluorescence-based quantitative PCR.

56. (Currently amended) The method of claim 54, wherein the probe is a FRET probe, or a dual-label hydrolysis probe comprising a fluorescence-reporter moiety and fluorescence-quencher moiety.

57. (Currently amended) The method of claim 56, wherein the FRET probe is one component of a real-time PCR ~~LightCycler™-type~~ ^{LightCycler™} hybridization probe pair.

58. (Currently amended) The method of claim 56, wherein the ~~dual-label~~ probe is a dual-label hydrolysis probe ~~TaqMan™-type~~ ^{TaqMan™} probe, or a molecular beacon-type probe.

59. (original) The method of claim 50, wherein at least one of the primers comprises a

CpG-specific probe.

60. (original) The method of claim 59, wherein the one primer is a scorpion-type primer comprising a CpG-specific probe that hybridizes to a target site within the scorpion primer extension product.

61. (Currently amended) A methylation detection kit useful for the detection of a methylated CpG-containing nucleic acid comprising a carrier means being compartmentalized to receive in close confinement therein one or more containers comprising:

(i) a modifying agent that modifies unmethylated cytosine to produce a converted nucleic acid;

(ii) primers for amplification of the converted nucleic acid;

(iii) primers for the amplification of control unmodified nucleic acid; and

(iv) a CpG-specific probe the detection of which is based on at least one of an amplification-, mediated-, or amplification product-mediated displacement or conformational change of the CpG-specific probe; or an amplification-mediated-, or amplification product-mediated displacement or conformational change of the probe ~~change in a property of the CpG-specific probe, or in a property thereof~~ in relation to another probe or a primer, wherein the CpG-specific probe distinguishes between modified unmethylated and methylated nucleic acid, and wherein the primers each may or may not distinguish between unmethylated and methylated nucleic acid.

62. (original) The kit of claim 61, wherein the modifying agent is bisulfite.

63. (original) The kit of claim 61 wherein the modifying agent converts cytosine residues to uracil residues.

64. (original) The kit of claim 61, wherein the CpG-specific probe, but not the primers for amplification of the converted nucleic acid, distinguishes between modified unmethylated and methylated nucleic acid.

65. (original) The kit of claim 61, wherein both the CpG-specific probe, and the primers for amplification of the converted nucleic acid, distinguish between modified unmethylated and methylated nucleic acid.

66. (original) The kit of claim 61, wherein the CpG-specific probe further comprises one or a plurality of fluorescence label moieties.

67. (Currently amended) The kit of claim 66, wherein the CpG-specific probe is a FRET probe, a real-time PCR LightCyclerTM-type hybridization probe, a dual-label hydrolysis probe, dual-labeled TaqManTM-type probe or a molecular beacon-type probe.

68. (original) The kit of claim 61, wherein one of the primers for amplification of the converted nucleic acid comprises the CpG-specific probe.

69. (original) The kit of claim 68, wherein the one primer is a scorpion-type primer

comprising a CpG-specific probe that hybridizes to a target site within the scorpion primer extension product.